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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/665,518	09/22/2003	Andre Stamm	31672-244620	5827

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EXAMINER	
SHEIKH, HUMERA N	

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1618	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/665,518	STAMM ET AL.	
	Examiner	Art Unit	
	Humera N. Sheikh	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 October 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-45* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-45* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the Application

Receipt of Request for Continued Examination (RCE) under 37 C.F.R. 1.114 and Applicant's Arguments/Remarks, all filed 10/19/2007 is acknowledged.

Claims 1-45 are pending in this action. No amendment(s) to the claims have been made with this response. Claims 1-45 are rejected.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 10/19/07 has been entered.

* * * * *

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-4, 6-17, 25-28 and 30-39 are rejected under 35 U.S.C. 103(a) as being unpatentable over Curtet *et al.* (hereinafter "Curtet") (US Pat. No. 4,895,726).

The instant invention is drawn to a capsule comprising a fenofibrate composition, said fenofibrate composition comprising fenofibrate, at least one hydrophilic polymer and at least one disintegrating agent, wherein the weight ratio of fenofibrate to hydrophilic polymer is between 1:10 and 4:1.

Curtet *et al.* ('726) teach a fenofibrate composition which is presented in the form of gelatin capsules and which is especially useful in the oral treatment of hyperlipidemia and hypercholesterolemia, whereby the composition comprises fenofibrate particles in combination with a solid surfactant, wherein the fenofibrate and solid surfactant have been co-micronized (see reference column 1, line 1 - col. 2, line 68) and Claim 1.

Curtet *et al.* teach that the recommended amount of fenofibrate is about 200 mg per therapeutic unit and the mean particle size of the fenofibrate is less than 15 microns, preferably less than 10 microns and particularly preferably less than 5 microns (col. 1, lines 50-66). Curtet teach that to obtain a powder which can be formulated into gelatin capsules, conventional filling, dispersing and flow-enhancing excipients, for example, lactose, starch, polyvinylpyrrolidone and

magnesium stearate may be added to the co-micronizate of fenofibrate and solid surfactant (col.1, line 67 through col. 2, line 4). Suitable disintegrants disclosed include crosslinked polyvinylpyrrolidone (col. 2, lines 36-37) and starch (col. 3, line 28).

Curtet teach a method for preparing a therapeutic composition comprising fenofibrate and a solid surfactant, which comprises (i) intimately mixing and then co-micronizing the fenofibrate and the solid surfactant, (ii) adding lactose and starch to the mixture obtained, (iii) converting the whole to granules in the presence of water, (iv) drying the granules until they contain no more than 1% of water, (v) grading the granules, (vi) adding polyvinylpyrrolidone and magnesium stearate to the graded granules and (vii) filling gelatin capsules with the mixture obtained in stage (vi). The mean particle size of the micronized mixture obtained is less than 15 microns (μm) (see reference column 2, lines 5-20).

Curtet teach overlapping amounts of fenofibrate and the hydrophilic polymer-polyvinylpyrrolidone, wherein the fenofibrate is present in an amount of 200 mg per therapeutic unit (col. 1, lines 50-51) and the polyvinylpyrrolidone is contained in an amount of 7 mg (col. 3, lines 21-32). The fenofibrate/solid surfactant mixture granules have a mean particle size of less than 15 μm (col. 1, lines 61-66).

According to Curtet, it is known that the micronization of an active principle is capable of improving the dissolution of the said active principle in vivo, and hence its bioavailability. It is also known that the addition of a surfactant excipient to a formulation of an active principle is capable of improving the absorption and consequently the bioavailability of the said active principle (col. 1, lines 28-34).

The fenofibrate composition can be presented in the form of gelatin capsules, which are especially useful in the oral treatment of hyperlipidemia and hypercholesterolemia (col. 1, lines 44-49).

Example 1 at column 2 demonstrates gelatin capsules containing drug, fenofibrate (20.0 kg), sodium laurly sulfate (0.7 kg), α-lactose monohydrate (10.1 kg), pregelatinized starch, disintegrant - cross-linked polyvinylpyrrolidone (0.7 kg) and magnesium stearate (0.5 kg).

Curtet *et al.* teach that the weight ratio of surfactant/fenofibrate will be between about 0.75/100 and 10.5/100 (col. 1, lines 59-60). Curtet *et al.* do not explicitly teach the claimed weight ratio of the fenofibrate/hydrophilic polymer. Curtet *et al.* also do not teach the claimed fenofibrate amounts/ranges. However, it is the position of the Examiner that Applicants have not demonstrated any unexpected or superior results attributable to the claimed weight ratio of the fenofibrate/polymer, nor the amounts of fenofibrate claimed, nor the particular hydrophilic polymer. Suitable or effective weight ratios of drug/polymer, surfactant/polymer and amounts ranges of drug/polymer could be determined by one of ordinary skill in the pharmaceutical art through routine or manipulative experimentation to obtain optimal results, as these are indeed variable parameters attainable within the art.

The instant invention would be *prima facie* obvious given the teachings of Curtet.

* * * * *

Claims 5, 18-24, 29 and 40-45 are rejected under 35 U.S.C. 103(a) as being unpatentable over Curtet *et al.* (hereinafter "Curtet") (US Pat. No. 4,895,726) as applied to claims 1-4, 6-17, 25-28 and 30-39 above and further in view of Kerč *et al.* (hereinafter "Kerč") (US Pat. No. 6,042,847).

The teachings of Curtet *et al.* are discussed above. Curtet teach a hydrophilic polymer, such as polyvinylpyrrolidone. Curtet do not teach the hydrophilic polymer - hydroxypropylcellulose.

Kerč *et al.* (847) teach a three-phase fenofibrate pharmaceutical formulation for daily peroral application, wherein the composition comprises cellulose ethers, such as hydroxypropylcellulose and whereby the compositions can be in the form of tablets or capsules. According to Kerč *et al.,* the cellulose ethers act as an agent for sustained and controlled release of the active ingredient (see reference column 1, lines 18-22); (col. 6, lines 4-28).

Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate hydrophilic polymers, such as hydroxypropylcellulose, as taught by Kerč *et al.* within the fenofibrate compositions of Curtet *et al.* One of ordinary skill in the art would be motivated to do so with a reasonable expectation of success because Kerč *et al.* explicitly teach a fenofibrate composition that comprises cellulose ethers, such as hydroxypropylcellulose that act as an agent for sustained and controlled release of the active ingredient. The expected result would be an improved, sustained or controlled release capsular fenofibrate composition for the treatment of high cholesterol levels.

Given the explicit teachings of Curtet *et al.* and Kerč *et al.*, the instant invention, when taken as a whole, would have been deemed *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

* * * * *

Response to Arguments

Applicant's arguments filed 10/19/07 have been fully considered but they are not persuasive.

Rejection under 35 U.S.C. 103(a) of claims 1-45 over Curtet ('726) in view of Kerč *et al.* ('847):

Applicant argued, "Neither Curtet nor Kerc disclose the claimed capsules having the claimed fenofibrate to polymer ratio of between 1:10 and 4:1. Neither Curtet nor Kerc provide any motivation to drastically reduce the weight ratio of fenofibrate to cross-linked PVP of 29:1 in Curtet to fall within the claimed range of fenofibrate to polymer of between 1:10 and 4:1. Kerc does not provide any motivation to modify the weight ratios of the components in Curtet to arrive at the claimed weight ratios."

Applicant's arguments have been considered, but were not persuasive. Admittedly, while the prior art teaches ratios of fenofibrate to polymer that are different than that claimed, the Examiner points out that the differences in ratio do not impart a patentable distinction over the explicit reference teachings. It remains the position of the Examiner that Suitable ratios could be determined by one of ordinary skill in the art through routine or manipulative experimentation to obtain optimal results, as these are variable parameters attainable within the art. Furthermore,

generally, differences in concentration will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller,* 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955). In the instant case, the prior art teaches a similar capsule as claimed, which is comprised of the same components (fenofibrate, polymers) and used for the same purpose (i.e., lowering cholesterol) as that of the Applicant. The determination of effective ratios is within the level of one of ordinary skill in the art.

Applicant argued, "Curtet fails to disclose the presence of both a hydrophilic polymer and disintegrating agent, because Curtet uses only a cross-linked PVP (i.e., a disintegrating agent)."

This argument has been considered, but was not rendered persuasive. Applicant appears to be relying on Preparation I disclosed at column 2, lines 28-39, wherein a disintegrant - cross-linked polyvinylpyrrolidone (X-PVP) is disclosed in combination with fenofibrate. However, also note that Preparation IV disclosed at column 3, lines 21-32 explicitly teaches a fenofibrate capsule comprising the incorporation of <u>both</u> a hydrophilic polymer - such as polyvinylpyrrolidone (PVP) and a disintegrating agent - starch. Hence, Curtet explicitly teaches the incorporation of both a hydrophilic polymer (i.e., polyvinylpyrrolidone) and a disintegrant (i.e., starch) and thus meets Applicant's claimed limitation. Moreover, the Examiner points out that the teachings of the prior art are not limited to the examples being exemplified therein. The reference is clearly suggestive of the inclusion of a combination of the active ingredient (fenofibrate), hydrophilic polymers (i.e., PVP) and disintegrant (i.e., X-PVP and/or starch) and thus is sufficient to read on the limitations instantly claimed.

Applicant argued, "The PTO asserts that Applicants failed to show the criticality of the claimed ratio. Applicants note that the Blouquin Declaration was not commented on by the Examiner, which shows the criticality of the claimed ratio."

Examiner notes that Applicants desire higher amounts of polymer to obtain increased or 'suprabioavailability'. However, the variation in the amounts of polymer instantly employed versus the level of hydrophilic polymer employed by the prior art, by itself, is insufficient to establish patentability of the claims. The prior art vividly teaches fenofibrate capsule formulations that comprise the same components claimed herein by Applicant, such as the hydrophilic polymer(s) and disintegrating agents. Moreover, Applicant's arguments directed to "suprabioavailability" do not establish the scope of claims being presented. For instance, at least independent claims, 1, 11 and 18 are silent in terms of any dissolution rates or bioavailability parameters. Furthermore, the preparations of Curtet are aimed at improving bioavailability of the active ingredient, i.e, fenofibrate (see Abstract).

Applicant argued, "Kerč teaches away form the claimed invention because Kerč teaches a three-phase pharmaceutical formulation with controlled release properties. One skilled in the art would not combine these references because Kerč's proposed modification (i.e., extended release) would change the principle of operation of Curtet's composition (i.e., relatively faster release than Kerč)."

This argument was fully considered but was not deemed persuasive. Applicant's themselves desire sustained or extended release as seen for instance, by the dissolution profile claimed in instant claim 7, which constitutes a controlled or sustained or extended release capsule formulation. Thus, the argument that "Curtet's formulation may achieve relatively faster

release than Kerč" was not persuasive since the formulations of Curtet are also controlled or sustained release formulations, as are those of Kerč.

The rejections of record have been maintained.

Conclusion

--No claims are allowed at this time.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Humera N. Sheikh whose telephone number is (571) 272-0604. The examiner can normally be reached on Monday, Tuesday, Thursday and Friday during regular business hours. (Wednesdays - Telework).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Hartley, can be reached on (571) 272-0616. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have any questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Art Unit 1615

January 20, 2008

HUMERA N SHEIKH
PRIMARY EXAMINER